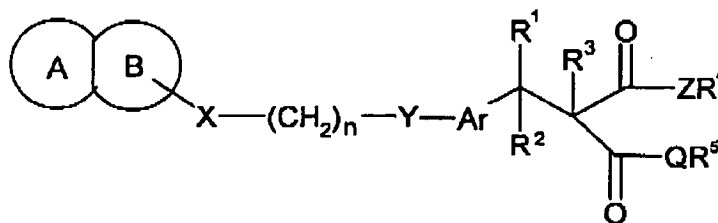


10/713,722

In the Claims:

1. (Currently Amended) A compound of formula I prepared for administration



(I)

wherein

ring A, fused to ring B, represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally be substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A may be saturated or contain one or more double bonds;

ring B, fused to ring A, represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally be substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring B may be saturated or contain one or more double bonds or may be aromatic;

X and Y are independently O, S, or NR<sup>6</sup> wherein R<sup>6</sup> represents hydrogen or C<sub>1-3</sub> alkyl;

Z represents O, S, or NR<sup>7</sup> wherein R<sup>7</sup> represents hydrogen, alkyl, aryl, or arylalkyl;

Q represents O, S, or NR<sup>7</sup> wherein R<sup>7</sup> represents hydrogen, alkyl, aryl, or arylalkyl;

R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

- 2 -

LV1 352105v1 09/22/05

PAGE 2/22 \* RCVD AT 9/22/2005 11:54:04 AM [Eastern Daylight Time] \* SVR:USPTO-EFAX-6/29 \* DNIS:2738300 \* CSID:609 896 1469 \* DURATION (mm-ss):07:42

10/713,722

$R^4$ ,  $R^5$  are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

Ar represents arylene, hetero arylene, or a divalent heterocyclic group each of which can optionally be substituted with one or more halogen,  $C_{1-6}$  alkyl, amino, hydroxy,  $C_{1-6}$  alkoxy or aryl; and

n is an integer ranging from 1 to 6.

2. (Original) The compound of claim 1, wherein

ring A is a 6-membered cyclic ring;

ring B is a 6-membered aromatic ring;

X and Y are independently O;

Z is O or  $NR^7$  wherein  $R^7$  represents hydrogen, alkyl, aryl, or arylalkyl;

Q is O or  $NR^7$  wherein  $R^7$  represents hydrogen, alkyl, aryl, or arylalkyl;

$R^1$ ,  $R^2$  and  $R^3$  are independently H or alkyl;

$R^4$  and  $R^5$  are independently H or alkyl;

Ar is an arylene group;

n is 2;

3. (Original) The compound of claim 1, wherein

ring A is a 6-membered cyclic ring;

ring B is benzene ring;

X and Y are independently O;

Z is O or  $NR^7$  wherein  $R^7$  represents hydrogen;

Q is O or  $NR^7$  wherein  $R^7$  represents hydrogen;

$R^1$ ,  $R^2$  and  $R^3$  are independently H;

$R^4$  and  $R^5$  are independently H or methyl;

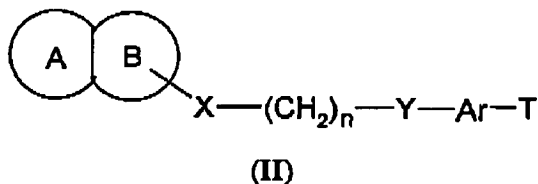
Ar is benzene group;

n is 2;

4. (Original) A compound of formula II wherein

10/713,722

ring A, ring B, X, Y, Ar and n are as defined in claim 1, and T is -CHO or - $R^1C=C(COOMe)_2$  wherein  $R^1$  is as defined in claim 1.



5. (Original) The compound according to claim 4 wherein:

ring A is a 6-membered cyclic ring;

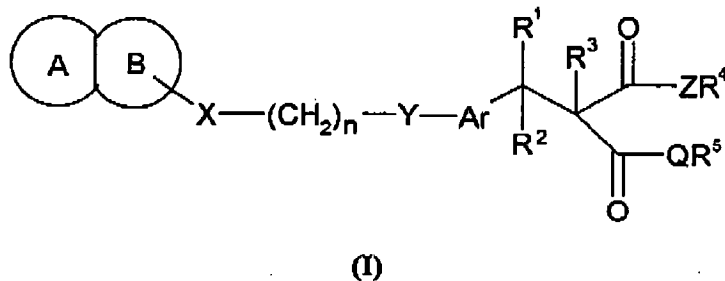
ring B is benzene ring;

X and Y are independently O;

Ar is benzene group;

n is 2;

6. (Original) A process for the preparation of a compound of formula I



wherein

ring A, fused to ring B, represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally be substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A may be saturated or contain one or more double bonds;

10/713,722

ring B, fused to ring A, represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally be substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring B may be saturated or contain one or more double bonds or may be aromatic;

X and Y are independently O, S, or  $\text{NR}^6$  wherein  $\text{R}^6$  represents hydrogen or  $\text{C}_{1-3}$  alkyl;

Z represents O, S, or  $\text{NR}^7$  wherein  $\text{R}^7$  represents hydrogen, alkyl, aryl, or arylalkyl;

Q represents O, S, or  $\text{NR}^7$  wherein  $\text{R}^7$  represents hydrogen, alkyl, aryl, or arylalkyl;

$\text{R}^1$ ,  $\text{R}^2$  and  $\text{R}^3$  are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

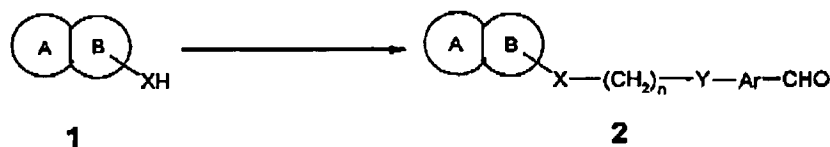
$\text{R}^4$ ,  $\text{R}^5$  are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

Ar represents arylene, hetero arylene, or a divalent heterocyclic group each of which can optionally be substituted with one or more halogen,  $\text{C}_{1-6}$  alkyl, amino, hydroxy,  $\text{C}_{1-6}$  alkoxy or aryl;

n is an integer ranging from 1 to 6;

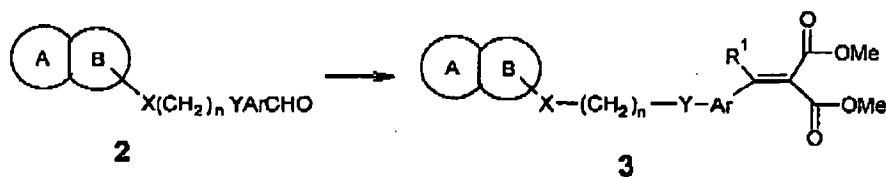
A stereoisomer, enantiomer, diastereomer, hydrate or pharmaceutically acceptable salt thereof comprising the steps of:

a) changing the compound of formula 1 to the benzaldehyde derivative 2;

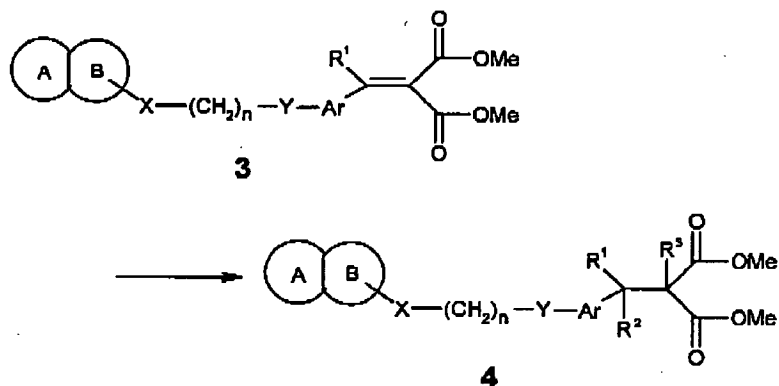


b) changing the aldehyde 2 to the benzylidene 3 by Knoevenagel condensation;

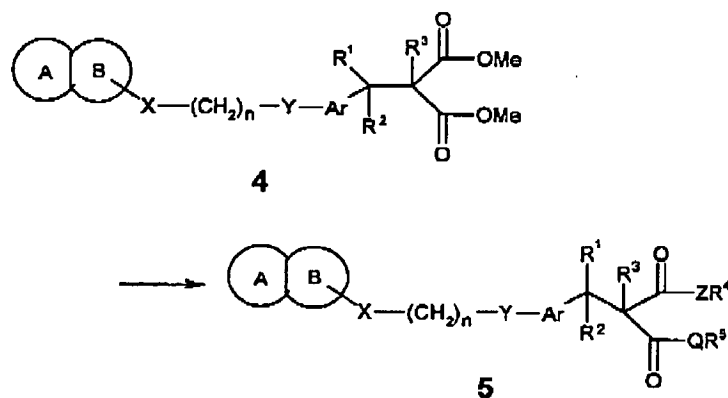
10/713,722



c) obtaining the dimethyl malonate 4 by catalytic hydrogenation of 3;



d) changing the dimethyl malonate 4 to other 1,3-dicarbonyl compounds 5.



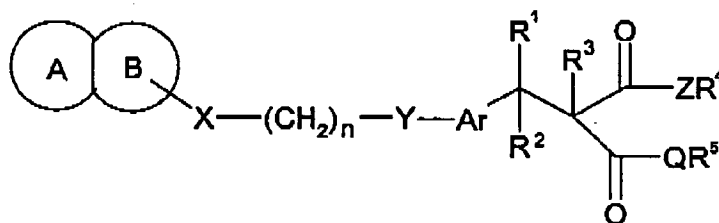
7. (Original) The process according to claim 6 wherein:

(a) the benzaldehyde derivative 2 is prepared by the reaction of compound 1 with p-bromoethoxy benzaldehyde in the presence of potassium hydroxide;

10/713,722

- (b) the Knoevenagel condensation is achieved by treating the benzaldehyde 2 with dimethyl malonate in the presence of a catalytic quantity of piperidinium acetate;
- (c) the catalytic hydrogenation is achieved by treating the benzylidene 3 with  $H_2$  in the presence of 5% palladium on carbon;
- (d) the other 1,3-dicarbonyl compounds 5 are prepared from 4 by hydrolysis or other conventional reactions.

8. (Original) A pharmaceutical composition for activating nuclear receptors comprising an effective amount of a compound of formula I



(I)

wherein

ring A, fused to ring B, represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally be substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A may be saturated or contain one or more double bonds;

ring B, fused to ring A, represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally be substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring B may be saturated or contain one or more double bonds or may be aromatic;

X and Y are independently O, S, or  $NR^6$  wherein  $R^6$  represents hydrogen or  $C_{1-3}$  alkyl;

- 7 -

LV1 352105v1 09/22/05

PAGE 7/22 \* RCVD AT 9/22/2005 11:54:04 AM [Eastern Daylight Time] \* SVR:USPTO-EFXRF-6/29 \* DNIS:2738300 \* CSID:609 896 1469 \* DURATION (mm-ss):07:42

10/713,722

Z represents O, S, or NR<sup>7</sup> wherein R<sup>7</sup> represents hydrogen, alkyl, aryl, or arylalkyl;

Q represents O, S, or NR<sup>7</sup> wherein R<sup>7</sup> represents hydrogen, alkyl, aryl, or arylalkyl;

R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

R<sup>4</sup>, R<sup>5</sup> are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

Ar represents arylene, hetero arylene, or a divalent heterocyclic group each of which can optionally be substituted with one or more halogen, C<sub>1-6</sub> alkyl, amino, hydroxy, C<sub>1-6</sub> alkoxy or aryl;

n is an integer ranging from 1 to 6; and

wherein the composition further comprises one or more pharmaceutically acceptable excipients, carriers or diluents.

9. (Original) The pharmaceutical composition according to claim 8, wherein the nuclear receptors comprise the Retinoid X Receptor (RXR), and the Peroxisome Proliferator-Activated Receptors (PPAR).

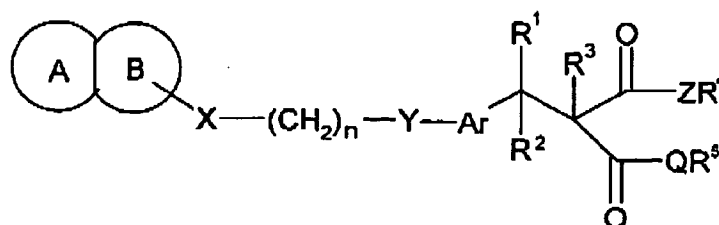
10. (Original) The pharmaceutical composition of claim 9 in unit dosage form, comprising from about 0.05 to about 100 mg of the active compound.

11. (Original) The pharmaceutical composition of claim 10 in unit dosage form, comprising from about 0.1 to about 50 mg of the active compound

12. (Original) The pharmaceutical composition of claim 9 which is suitable for administration by an oral, nasal, transdermal, pulmonary, or parenteral route.

13. (Currently Amended) A method of treating or preventing a condition mediated by at least one nuclear-receptor Peroxisome Proliferator-Activated Receptor (PPAR), comprising administering to a subject in need thereof an effective amount of a compound of formula I

10/713,722



(I)

wherein

ring A, fused to ring B, represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally be substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A may be saturated or contain one or more double bonds;

ring B, fused to ring A, represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally be substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring B may be saturated or contain one or more double bonds or may be aromatic;

X and Y are independently O, S, or  $NR^6$  wherein  $R^6$  represents hydrogen or  $C_{1-3}$  alkyl;

Z represents O, S, or  $NR^7$  wherein  $R^7$  represents hydrogen, alkyl, aryl, or arylalkyl;

Q represents O, S, or  $NR^7$  wherein  $R^7$  represents hydrogen, alkyl, aryl, or arylalkyl;

$R^1$ ,  $R^2$  and  $R^3$  are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

$R^4$ ,  $R^5$  are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;



10/713,722

Ar represents arylene, hetero arylene, or a divalent heterocyclic group each of which can optionally be substituted with one or more halogen, C<sub>1-6</sub> alkyl, amino, hydroxy, C<sub>1-6</sub> alkoxy or aryl; and

n is an integer ranging from 1 to 6.

14-16. (Canceled)

17. (Currently Amended) A method according to claim [[15]] 13 wherein said condition is selected from the group consisting of type 1 diabetes, type 2 diabetes, dyslipidemia, syndrome X, cardiovascular disease, atherosclerosis, hypercholesteremia, and obesity.

18. (Currently Amended) The method according to claim [[15]] 17, wherein the effective amount of the compound is in the range of from about 0.05 to about 100 mg/kg body weight per day.

19. (Currently Amended) The method according to claim [[15]] 17, wherein the effective amount of the compound is in the range of from about 0.1 to about 50 mg/kg body weight per day.

\* \* \*